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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,337	12/17/2001	Todd J. Vision	19603/4040 (CRF D-2630)	5690

7590 11/07/2005

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EXAMINER
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GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 11/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/023,337	Applicant(s) VISION ET AL.	
	Examiner Jeanine A. Goldberg	Art Unit 1634	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-17, 21-23 and 28-49 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17, 21-23 and 28-49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

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### DETAILED ACTION

1. This action is in response to the papers filed August 26, 2005.
2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 26, 2005 has been entered.
3. Currently, claims 1-17, 21-23, 28-49 are pending.
4. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.
5. Any objections and rejections not reiterated below are hereby withdrawn.
6. This action contains new grounds of rejection.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-4, 9-17, 21, 28-30, 37, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Monforte et al. (US Pat. 5,700,642, December 23, 1997).

Adams et al. (herein referred to as Adams) teaches a method for performing amplifications of nucleic acid on supports. Adams teaches that target nucleic acid sequence in a test sample is amplified, detected, and can be quantified, using pairs of primer attached to a surface contacting the sample and optionally other chemical reagents (col. 12, lines 60-66). In example 1, Adams teaches detection of an elongation product (col. 22). The primer is immobilized on an epoxy silane derivatized solid support by a 5' amino group (col. 22, lines 50-55)(limitations of Claim 1a, 29). Spacer groups of hexaethylene-glycol are included during synthesis of the primer to eliminate stearic hindrance during the annealing reaction (limitations of Claim 21). The spacer region is introduced into the synthesized primer prior to amino group addition, resulting in a calculated spacer region length of 25 angstroms (col. 22, lines 55-58)(limitations of claim 14-17). Adams further reaches that NH<sub>2</sub>-C<sub>6</sub> linkers may be used on the primers such that the primers carry a primary amine group linked by a six carbon chain at their

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5' ends (col. 24)(limitations of Claim 18). The primer is allowed to anneal to the target sequence of the test sample and extended to form an elongation product extending from the immobilized primer and which is complementary to the target nucleic acid sequence (col. 22, lines 60-66)(limitations of Claim 1b, c). The reaction mixture is washed from the reaction surface and the immobilized amplification product detected (limitations of claim 1d). When amplification conditions are imposed, amplified target nucleic acid sequence, also referred to herein as polynucleotide, is formed and attached to said surface by extension from the primers so attached (col. 13, lines 4-6). The amplificate so formed can be detected (col. 13, lines 10-13). Labeling techniques include using a detectable probe after the amplification phase of the analysis is complete (col. 13, lines 13-15)(limitations of Claim 1e, f). Adams teaches detecting the label immobilized on the solid substrate indicating the presence or absence of the target nucleic acid molecule in the sample. Adams teaches that when detection scheme is fluorescence of a fluorogenic substance, such fluorescence can be induced by irradiating the surface bound amplificate with excitation radiation (col. 13, lines 20-25)(limitations of Claim 41). Adams teaches using the human beta-globin gene (limitations of Claim 2, 3)(col. 24, lines 50-65). Adams teaches that the invention can be used to detect genetic abnormalities, such as mutations that are associated with specific disease, such as cystic fibrosis, or a genetic marker for cancer such as mutated BRCA1. The methods can also be used to detect viral, bacterial and yeast nucleic acids from pathogenic organisms indicative of infection (col. 5, lines 60-70)(limitations of Claim 4, 9-12). Adams further teaches that the methods can be used in forensic

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medicine (limitations of Claim 13). Adams teaches that the solid support encompasses beads, membranes, silicon, silane and silicate supports (col. 7, lines 40-45)(limitations of Claim 28). Adams teaches that the surface can contain concave or convex areas that would be particularly suited to provide for the analysis of multiple samples , ie. a microwell (col. 7, lines 55-60)(limitations of Claim 37).

Adams does not specifically teach the structure of the 5-Amino Modifier C6 Spacer or a spacer phosphoramidite 18. Adams further does not specifically teach functionalizing with an amine compound such as 3-aminopropyltrimethylsilane (limitations of Claim 30).

However, Monforte et al teaches a method of amino-modified oligonucleotides for use in attaching to a solid support using 5'-amino-modifier C6, from Glen Research, Sterling, VA. The instant specification also appears to use the Glen Research 5'-Amino-modifier C6. The Glen Research 5'-amino-modifier C6 has the same chemical formula as recited and required by the instant claims. Monforte teaches that the amino-modified oligonucleotides are used for attaching to a solid support. Further, glass slides may be activated for coupling to amino-functionalized oligonucleotides. The glass slide is exposed to 3-aminopropyltrimethoxysilane (col. 32, lines 13-16)(limitations of Claim 30).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have attached the oligonucleotides to the support using known chemical structures for the linkers. Since Monfote teaches the structures of the spacers which may be easily used for attaching oligonucleotides to a support, the

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ordinary artisan would have been motivated to have used these structures to attach the oligonucleotides to the support. Further, the 5' amino-modifier C6 from Glen Research was commercially available at a reasonable cost and using an available linking agent would have been obvious to the ordinary artisan at the time the invention was made.

9. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Monforte et al. (US Pat. 5,700,642, December 23, 1997) as applied to claims 1-4, 9-17, 21, 28-29, 37, 41 above and further in view of Hall (US Pat. 5,475,098).

While Adams suggest that the method can be used to detect viral, bacterial and yeast nucleic acids from pathogenic organisms, Adams does not specifically teach detecting *E. coli*.

However, Hall teaches nucleic acids oligonucleotides useful for detecting *E. coli*.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the method of Adams in view of Monforte for detecting nucleic acids to detect the specific nucleic acids taught by Hall. The ordinary artisan would have been motivated to have detect *E. coli* for the expect benefit of rapidly and specifically detecting the infections bacteria *E. coli*.

10. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Monforte et al. (US Pat. 5,700,642,



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December 23, 1997) as applied to claims 1-4, 9-17, 21, 28-29, 37, 41 above and further in view of Springer (US Pat. 5,489,513).

While Adams suggest that the method can be used to detect viral, bacterial and yeast nucleic acids from pathogenic organisms, Adams does not specifically teach detecting *Candida albicans*.

However, Springer teaches nucleic acids oligonucleotides useful for detecting *Candida albicans*.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the method of Adams in view of Monforte for detecting nucleic acids to detect the specific nucleic acids taught by Springer. The ordinary artisan would have been motivated to have detect *Candida albicans* for the expect benefit of rapidly and specifically detecting the infections fungus *Candida albicans*.

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Monforte et al. (US Pat. 5,700,642, December 23, 1997) as applied to claims 1-4, 9-17, 21, 28-29, 37, 41 above and further in view of Respass (US Pat. 5,599,662).

While Adams suggest that the method can be used to detect viral, bacterial and yeast nucleic acids from pathogenic organisms, Adams does not specifically teach detecting *human immunodeficiency virus (HIV)*.



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However, Respass teaches nucleic acids oligonucleotides useful for detecting HIV.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the method of Adams in view of Monforte for detecting nucleic acids to detect the specific nucleic acids taught by Respass. The ordinary artisan would have been motivated to have detect HIV for the expect benefit of rapidly and specifically detecting the infections virus HIV.

12. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Monforte et al. (US Pat. 5,700,642, December 23, 1997) as applied to claims 1-4, 9-17, 21, 28-29, 37, 41 above and further in view of Wataya (US Pat. 5,792,609)

While Adams suggest that the method can be used to detect viral, bacterial and yeast nucleic acids from pathogenic organisms, Adams does not specifically teach detecting *Plasmodium ovale*.

However, Wataya teaches nucleic acids oligonucleotides useful for detecting *Plasmodium ovale*.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the method of Adams in view of Monforte for detecting nucleic acids to detect the specific nucleic acids taught by Wataya. The ordinary artisan would have been motivated to have detect *Plasmodium ovale* for the

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expect benefit of rapidly and specifically detecting the infections fungus *Plasmodium ovale*.

13. Claims 31-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Monforte et al. (US Pat. 5,700,642, December 23, 1997) as applied to claims 1-4, 9-17, 21, 28-30, 37, 41 above and further in view of Fulcrand et al. (US Pat. 6,319,674, November 2001).

Adams and Monforte does not specifically teach using particular olefin monomers or particular substrates.

However, Fulcrand et al. (herein referred to as Fulcrand) teaches methods for the covalent attachment of ligands to a surface. These reactions are typically performed by reaction of an active functional group on the ligand with an activated functional group on the surface. Functional groups include treating the surface of an organic support with N-(2-aminoethyl)-3-aminopropyltrimethoxysilane or 3-aminopropyltriethoxysilane with the amino group as an attachment point (col. 2, lines 37-40)(limitations of Claim 30). Fulcrand teaches that the surface of the support may be glass, silica, magnesium sulfate, natural polymeric material such as polyacrylamide, polyacrylate, polyethylene, polypropylene, for example (see complete list on col. 1, lines 20-40)(limitations of Claim 36). Moreover, the surface may be treated to attach the first portion of the linking group. For surface comprised of silicon oxide groups, one technique for introducing siloxyl groups onto the surface involves reactive hydrophilic moieties on the surface. For example an olefin that may be converted to a hydroxyl

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group is appropriate (col. 14, lines 45-65)(limitations of Claims 31-35). Fulcrand further teaches a number of ways that the functionalization is attached. The silyl functionality can be a trichlorosilyl functionality, or tri(lower) alkoxysilyl functionality such as trimethoxysilyl or tiethoxysilyl (col. 15). The mixtures thereof, may include any of the functional groups identified by the instant claims.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the attachment means for attaching the primer of Adams in view of Monforte to the solid support using the teachings of Fulcrand. Fulcrand teaches a wide variety of covalent linkages which require various functional groups on the probes and on the surfaces. The ordinary artisan would have been motivated to have attached the instant probes to the solid support using any well known method taught in the art absent unexpected results.

14. Claims 38-40, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Monforte as applied to claims 1-4, 9-17, 21, 28-30, 37, 41 above and further in view of George (US Pat. 5,728,526).

Adams does not specifically teach using an extension reaction comprising all dNTP and dITP and dUTP or particular polymerase.

However, George teaches different nucleotides which can be used in extension are deoxythymidine triphosphate (dTTP); deoxyadenosine triphosphate (dATP); deoxyguanosine triphosphate (dGTP); and deoxycytidine triphosphate (dCTP). On the

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other hand, when the target nucleic acid sequence is RNA, the four different nucleotides are uridine triphosphate (UTP); adenosine triphosphate (ATP); guanosine triphosphate (GTP); and cytidine triphosphate (CTP). Alternatively, deoxyuridine triphosphate (dUTP), deoxyinosine triphosphate (dITP), inosine triphosphate (ITP) or any other modified base may replace one of the four nucleotides or may be included along with the four nucleotides (col. 13, lines 5-25). George further teaches that the polymerizing agent for extension may include E. coli DNA polymerase to form complementary sequence to the target (col. 13, lines 35-45)(limitation of Claim 39). Further, George teaches that hybridization takes place at temperatures of 63-68C. Thus, probe temperatures which are greater are more preferable for stability and detection. Finally, George teaches polynucleotides may be labeled with fluorescent dyes, such as fluorescein, Texas Red, for example.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the teachings of Adams to include a composition of all four nucleotides along with inosine and deoxyuridine for the benefits of modified bases taught by George. Further, the ordinary artisan would have been motivated to have used well known polymerases in the method of Adams such as the polymerases taught by George which function to extend nucleic acids. Adams specifically teaches using a thermostable polymerase, however fails to specifically teach which polymerase was used. Therefore, using any of the thermostable polymerases taught by George would have been obvious to the ordinary artisan at the time the invention was made. Finally, Adams does not specifically teach the labeling means for

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the nucleic acid probes. However, George specifically teaches well known labeling means which would be useful for labeling the probes. Therefore, the ordinary artisan would have been motivated to have labeled the probe with a detectable probe which was detectable with fluorescence.

15. Claims 22-23, 43-47, 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Nie (US Pat 6,255,050, July 2001).

Adams et al. (herein referred to as Adams) teaches a method for performing amplifications of nucleic acid on supports. Adams teaches that target nucleic acid sequence in a test sample is amplified, detected, and can be quantified, using pairs of primer attached to a surface contacting the sample and optionally other chemical reagents (col. 12, lines 60-66). In example 1, Adams teaches detection of an elongation product (col. 22). The primer is immobilized on an epoxy silane derivatized solid support by a 5' amino group (col. 22, lines 50-55)(limitations of Claim 1a, 29). Spacer groups of hexaethylene-glycol are included during synthesis of the primer to eliminate steric hindrance during the annealing reaction (limitations of Claim 21). The spacer region is introduced into the synthesized primer prior to amino group addition, resulting in a calculated spacer region length of 25 angstroms (col. 22, lines 55-58)(limitations of claim 14-17). Adams further teaches that NH<sub>2</sub>-C<sub>6</sub> linkers may be used on the primers such that the primers carry a primary amine group linked by a six carbon chain at their 5' ends (col. 24)(limitations of Claim 18). The primer is allowed to anneal to the target

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sequence of the test sample and extended to form an elongation product extending from the immobilized primer and which is complementary to the target nucleic acid sequence (col. 22, lines 60-66)(limitations of Claim 1b, c). The reaction mixture is washed from the reaction surface and the immobilized amplification product detected (limitations of claim 1d). When amplification conditions are imposed, amplified target nucleic acid sequence, also referred to herein as polynucleotide, is formed and attached to said surface by extension from the primers so attached (col. 13, lines 4-6). The amplificate so formed can be detected (col. 13, lines 10-13). Labeling techniques include using a detectable probe after the amplification phase of the analysis is complete (col. 13, lines 13-15)(limitations of Claim 1e, f). Adams teaches detecting the label immobilized on the solid substrate indicating the presence or absence of the target nucleic acid molecule in the sample. Adams teaches that when detection scheme is fluorescence of a fluorogenic substance, such fluorescence can be induced by irradiating the surface bound amplificate with excitation radiation (col. 13, lines 20-25)(limitations of Claim 41). Adams teaches using the human beta-globin gene (limitations of Claim 2, 3)(col. 24, lines 50-65). Adams teaches that the invention can be used to detect genetic abnormalities, such as mutations that are associated with specific disease, such as cystic fibrosis, or a genetic marker for cancer such as mutated BRCA1. The methods can also be used to detect viral, bacterial and yeast nucleic acids from pathogenic organisms indicative of infection (col. 5, lines 60-70)(limitations of Claim 4, 9-12). Adams further teaches that the methods can be used in forensic medicine (limitations of Claim 13). Adams teaches that the solid support encompasses

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beads, membranes, silicon, silane and silicate supports (col. 7, lines 40-45)(limitations of Claim 28). Adams teaches that the surface can contain concave or convex areas that would be particularly suited to provide for the analysis of multiple samples , ie. a microwell (col. 7, lines 55-60)(limitations of Claim 37).

Adams does not specifically teach the structure of the 5-Amino Modifier C6 Spacer or a spacer phosphoramidite 18.

However, Nie et al. teaches modifying two 18mer oligonucleotides with 5'-amino group linkers. The amino group linkers/spacers included Spacer phosphoramidite 18-DMT with the chemical formula provided by the instant claims. Nie teaches the spacer was purchased from Glen Research (Sterling, VA), the same source as the spacer from the instant specification. Nie then immobilizes the oligonucleotides to a solid support.

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have attached the oligonucleotides to the support using known chemical structures for the linkers. Nie teaches the structures of the spacers which may be easily used for attaching oligonucleotides to a support, the ordinary artisan would have been motivated to have used these structures to attach the oligonucleotides to the support. Further, the hexaethylene glycol spacer phosphoramidite from Glen Research was commercially available at a reasonable cost and using an available linking agent would have been obvious to the ordinary artisan at the time the invention was made.



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16. Claims 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. (US Pat. 6,060,288, May 2000) in view of Nie (US Pat. 6,255,050, July 2001) as applied to claims 22-23, 43-47, 49 above and further in view of George (US Pat. 5,728,526).

Adams and Nie do not specifically teach using an extension reaction comprising all dNTP and dITP and dUTP or particular polymerase.

However, George teaches different nucleotides which can be used in extension are deoxythymidine triphosphate (dTTP); deoxyadenosine triphosphate (dATP); deoxyguanosine triphosphate (dGTP); and deoxycytidine triphosphate (dCTP). On the other hand, when the target nucleic acid sequence is RNA, the four different nucleotides are uridine triphosphate (UTP); adenosine triphosphate (ATP); guanosine triphosphate (GTP); and cytidine triphosphate (CTP). Alternatively, deoxyuridine triphosphate (dUTP), deoxyinosine triphosphate (dITP), inosine triphosphate (ITP) or any other modified base may replace one of the four nucleotides or may be included along with the four nucleotides (col. 13, lines 5-25). George further teaches that the polymerizing agent for extension may include E. coli DNA polymerase to form complementary sequence to the target (col. 13, lines 35-45)(limitation of Claim 39). Further, George teaches that hybridization takes place at temperatures of 63-68C. Thus, probe temperatures which are greater are more preferable for stability and detection. Finally, George teaches polynucleotides may be labeled with fluorescent dyes, such as fluorescein, Texas Red, for example.

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Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have modified the teachings of Adams in view of Nie to include a composition of all four nucleotides along with inosine and deoxyuridine for the benefits of modified bases taught by George. Further, the ordinary artisan would have been motivated to have used well known polymerases in the method of Adams such as the polymerases taught by George which function to extend nucleic acids. Adams specifically teaches using a thermostable polymerase, however fails to specifically teach which polymerase was used. Therefore, using any of the thermostable polymerases taught by George would have been obvious to the ordinary artisan at the time the invention was made. Finally, Adams does not specifically teach the labeling means for the nucleic acid probes. However, George specifically teaches well known labeling means which would be useful for labeling the probes. Therefore, the ordinary artisan would have been motivated to have labeled the probe with a detectable probe which was detectable with fluorescence.

### ***Conclusion***

**17. No claims allowable over the art.**

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272- 0745.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

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applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

A handwritten signature in cursive script, appearing to read "J. Goldberg", is positioned above the printed name.

**Jeanine Goldberg**

**Primary Examiner**

November 3, 2005